Teclistamab, Daratumumab, and Pomalidomide in Patients With Relapsed/Refractory Multiple Myeloma: Results From the MajesTEC-2 Cohort A and TRIMM-2 Studies

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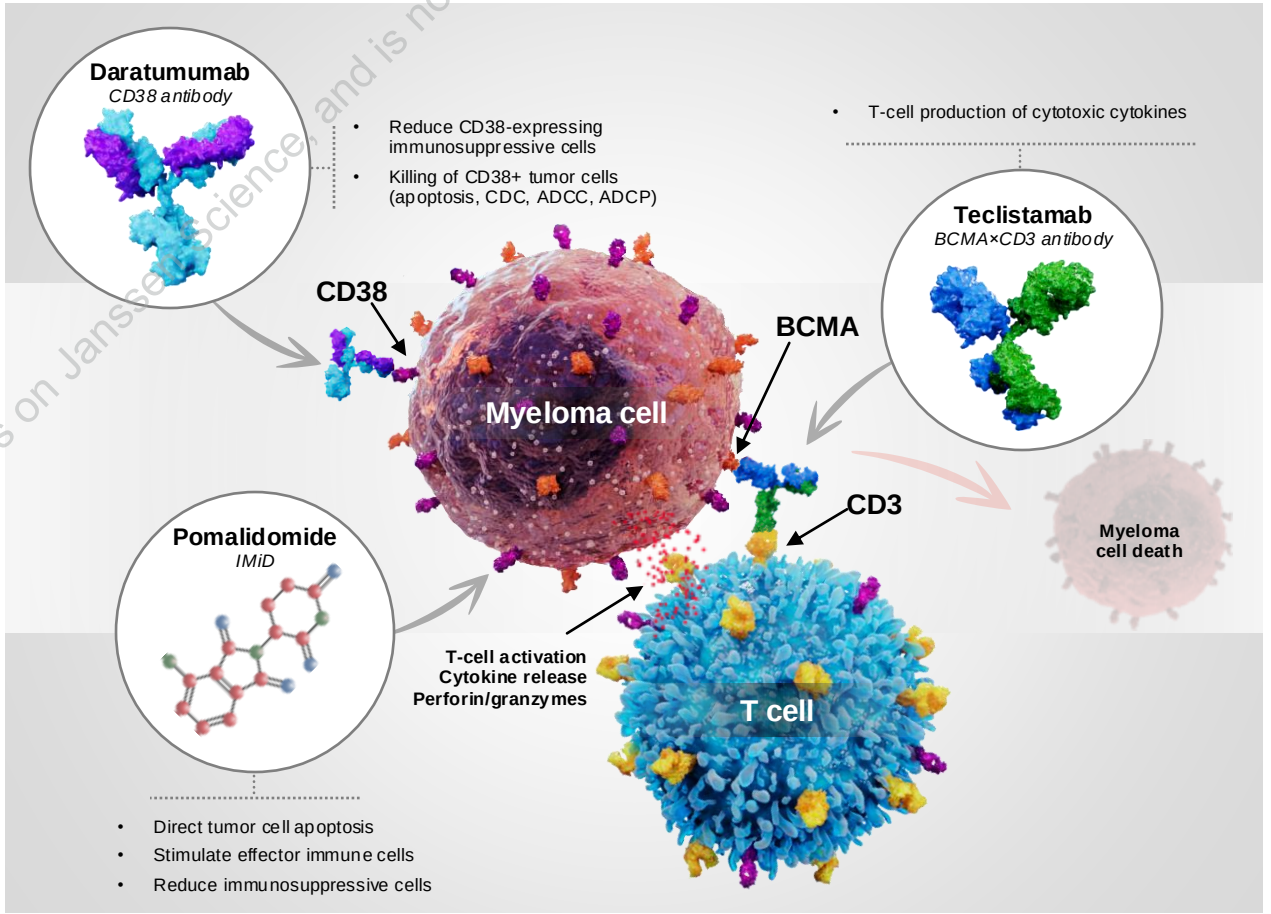
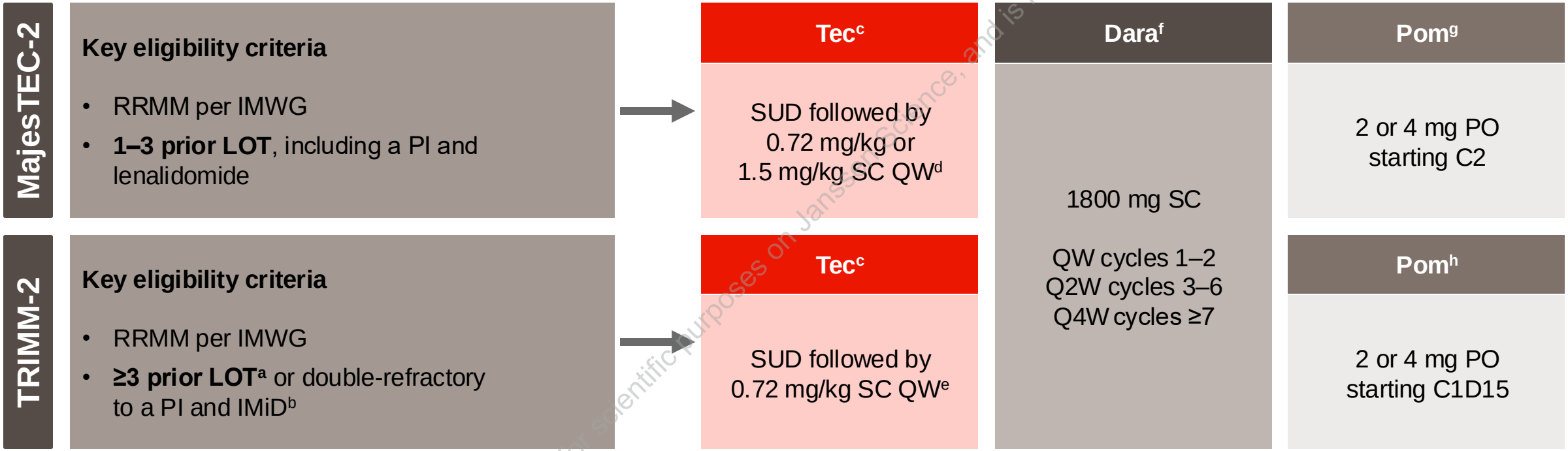
Tec-Dara-Pom: Fully Immune-Based Combination Therapy

- Teclistamab is the first approved BCMA×CD3 bispecific antibody with weight-based dosing for triple-class exposed RRMM[1-3]
- Daratumumab, combined with teclistamab, targets myeloma through direct cytotoxicity and enhanced immune effector function – potentially improving the antitumor activity of teclistamab[4]
- Tec + Dara in combination with lenalidomide has shown promising early efficacy and manageable safety in patients with NDMM[5] or 1–3 prior LOT[6]
- We present preliminary safety and efficacy for Tec-Dara-Pom in patients with RRMM in the phase 1b MajesTEC-2 and TRIMM-2 studies



ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; BCMA, B-cell maturation antigen; CDC, complement-dependent cytotoxicity; Dara, daratumumab; IMiD, immunomodulatory drug; LOT, line of therapy; NDMM, newly diagnosed multiple myeloma; Pom, pomalidomide; RRMM, relapsed/refractory multiple myeloma; Tec, teclistamab. 1. TECVAYLI (teclistamab). Summary of product characteristics. Leiden, Netherlands: Janssen Biologics BV; 2024. 2. TECVAYLI (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2024. 3. Moreau P, et al. *N Engl J Med* 2022;387:495-505. 4. Vishwamitra D, et al. Presented at ASH; December 7–10, 2024; San Diego, CA, USA. Oral #594. 5. Touzeau C, et al. Presented at ASCO; May 31–June 4, 2024; Chicago, IL, USA & Virtual. Oral #7506. 6. Searle E, et al. Presented at ASH; December 10–13, 2022; New Orleans, LA, USA. Oral #160.

Phase 1b MajesTEC-2 and TRIMM-2 Tec-Dara-Pom Cohorts



- **Key objectives:** Safety, antitumor activity, PK, PD, immunogenicity

MajesTEC-2: NCT04722146. TRIMM-2: NCT04108195. [a]Including a PI and an IMiD. [b]Including lenalidomide. [c]2 SUDs before first full dose; premedication included glucocorticoid, antihistamine, and antipyretic at SUD and first full dose. [d]Treatment doses of Tec could be adjusted from C3 onwards based on study safety evaluation team decision (eg, Q2W dosing). [e]Patients could switch to Q2W and then to Q4W dosing based on depth and duration of response. 1 patient in this cohort received Tec 0.75 mg/kg. [f]Given with 1-week (MajesTEC-2) or 2-week (TRIMM-2) corticosteroid taper (steroid-free administration). [g]Dexamethasone 40 mg PO given QW in C2–C4. [h]Dexamethasone 40 mg PO or IV given on D15 and D22 of C1, and QW in C2–C4. C, cycle; D, day; Dara, daratumumab; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; IV, intravenous; LOT, line of therapy; PD, pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics; PO, orally; Pom, pomalidomide; PR, partial response; Q2W, every other week; Q4W, every 4 weeks; QW, weekly; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; SUD, step-up dose; Tec, teclistamab; VGPR, very good partial response.

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Tec-Dara-Pom in MajesTEC-2 and TRIMM-2: Baseline Characteristics

Characteristic	MajesTEC-2 (n=17)	TRIMM-2 (n=10)	All patients (N=27)
Median age, years (range)	62 (35–74)	58 (37–79)	62 (35–79)
Male, n (%)	11 (64.7)	5 (50.0)	16 (59.3)
Race, n (%)			
White	11 (64.7)	8 (80.0)	19 (70.4)
Black/African American	2 (11.8)	1 (10.0)	3 (11.1)
Asian	1 (5.9)	0	1 (3.7)
Not reported	3 (17.6)	1 (10.0)	4 (14.8)
ECOG PS score ≤1, n (%)	17 (100)	10 (100)	27 (100)
EMD, n (%)[a]	0	3 (30.0)	3 (11.1)
High cytogenetic risk, n (%)[b]	4 (26.7)	3 (33.3)	7 (29.2)
ISS stage, n (%)[c]			
I	9 (56.3)	6 (60.0)	15 (57.7)
II	5 (31.3)	3 (30.0)	8 (30.8)
III	2 (12.5)	1 (10.0)	3 (11.5)
Prior SCT, n (%)	15 (88.2)	9 (90.0)	24 (88.9)
Median prior LOT, n (range)	1 (1–4)	4 (3–16)	2 (1–16)
Prior anti-CD38, n (%)[d]	3 (17.6)	8 (80.0)	11 (40.7)
Prior anti-BCMA, n (%)	0	3 (30.0)	3 (11.1)
Triple-class refractory, n (%)[e]	0	7 (70.0)	7 (25.9)

- Patients in TRIMM-2 were more heavily pretreated than those in MajesTEC-2
  - Median prior LOT 4 (range, 3–16) vs 1 (range, 1–4)
  - Prior anti-CD38 exposure 80.0% vs 17.6%
  - Prior anti-BCMA exposure 30.0% vs 0

[a]Assessed if history of plasmacytomas or if clinically indicated at screening (paraskeletal lesions not considered EMD). [b]del(17p), t(4;14), and/or t(14;16); n=24 (MajesTEC-2, n=15; TRIMM-2, n=9). [c]n=26 (MajesTEC-2, n=16; TRIMM-2, n=10). [d]All patients with prior anti-CD38 exposure had received daratumumab; 1 patient from TRIMM-2 had also received isatuximab. [e]≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. BCMA, B-cell maturation antigen; Dara, daratumumab; ECOG PS, Eastern Cooperative Oncology Group performance status; EMD, extramedullary disease; IMiD, immunomodulatory drug; ISS, International Staging System; LOT, line of therapy; mAb, monoclonal antibody; PI, proteasome inhibitor; Pom, pomalidomide; SCT, stem cell transplantation; Tec, teclistamab.

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Tec-Dara-Pom in MajesTEC-2 and TRIMM-2: Hematologic TEAEs

	MajesTEC-2 (1–3 prior LOT) (n=17)		TRIMM-2 (≥3 prior LOT) (n=10)		All patients (N=27)	
Median follow-up, months (range)	16.2 (0.5–34.5)		38.3 (1.2–39.6)		25.8 (0.5–39.6)	
	Any Grade	**Grade 3/4**	**Any Grade**	**Grade 3/4**	**Any Grade**	**Grade 3/4**
Any TEAE	17 (100)	16 (94.1)	10 (100)	10 (100)	27 (100)	26 (96.3)
Hematologic[a]						
Neutropenia	15 (88.2)	15 (88.2)	6 (60.0)	6 (60.0)	21 (77.8)	21 (77.8)
Thrombocytopenia	7 (41.2)	1 (5.9)	3 (30.0)	2 (20.0)	10 (37.0)	3 (11.1)
Anemia	7 (41.2)	4 (23.5)	1 (10.0)	1 (10.0)	8 (29.6)	5 (18.5)
Lymphopenia	3 (17.6)	3 (17.6)	3 (30.0)	3 (30.0)	6 (22.2)	6 (22.2)
Leukopenia	4 (23.5)	2 (11.8)	2 (20.0)	1 (10.0)	6 (22.2)	3 (11.1)
Febrile neutropenia	1 (5.9)	1 (5.9)	2 (20.0)	2 (20.0)	3 (11.1)	3 (11.1)

- The most common grade 3/4 hematologic TEAEs were neutropenia (77.8%), lymphopenia (22.2%), and anemia (18.5%)
- No new safety signals seen vs known safety profiles of individual drugs

AEs were graded by CTCAE v5.0.
[a]Hematologic TEAEs in >1 patient in either study.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; Dara, daratumumab; LOT, line of therapy; Pom, pomalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab.

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Tec-Dara-Pom in MajesTEC-2 and TRIMM-2: Nonhematologic TEAEs

	MajesTEC-2 (1–3 prior LOT) (n=17)		TRIMM-2 (≥3 prior LOT) (n=10)		All patients (N=27)	
Median follow-up, months (range)	16.2 (0.5–34.5)		38.3 (1.2–39.6)		25.8 (0.5–39.6)	
	Any Grade	**Grade 3/4**	**Any Grade**	**Grade 3/4**	**Any Grade**	**Grade 3/4**
Any TEAE	17 (100)	16 (94.1)	10 (100)	10 (100)	27 (100)	26 (96.3)
Nonhematologic[a]						
Cough	11 (64.7)	0	5 (50.0)	0	16 (59.3)	0
CRS	8 (47.1)	0	7 (70.0)	0	15 (55.6)	0
Hypokalemia	3 (17.6)	3 (17.6)	4 (40.0)	1 (10.0)	13 (48.1)	4 (14.8)
Pyrexia	8 (47.1)	0	5 (50.0)	0	13 (48.1)	0
Diarrhea	9 (52.9)	2 (11.8)	2 (20.0)	0	11 (40.7)	2 (7.4)
Fatigue	7 (41.2)	1 (5.9)	4 (40.0)	0	11 (40.7)	1 (3.7)
Injection site erythema	7 (41.2)	0	3 (30.0)	0	10 (37.0)	0

- All CRS events were grade 1/2 and resolved
- 1 case of grade 1 ICANS, which resolved
- 4 patients discontinued study treatment due to nonfatal TEAEs[b]

AEs were graded by CTCAE v5.0, except for CRS and ICANS (graded per ASTCT). [a]Nonhematologic TEAEs in ≥30% of patients in either study. [b]Preferred Terms of decreased appetite, diarrhea, weight decreased, colitis, viral upper respiratory tract infection, and bronchopulmonary aspergillosis (multiple terms per patient possible; treatment discontinuation due to grade 5 events summarized on next slide). AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; Dara, daratumumab; ICANS, immune effector cell–associated neurotoxicity syndrome; LOT, line of therapy; Pom, pomalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab.

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Tec-Dara-Pom in MajesTEC-2 and TRIMM-2: Infections

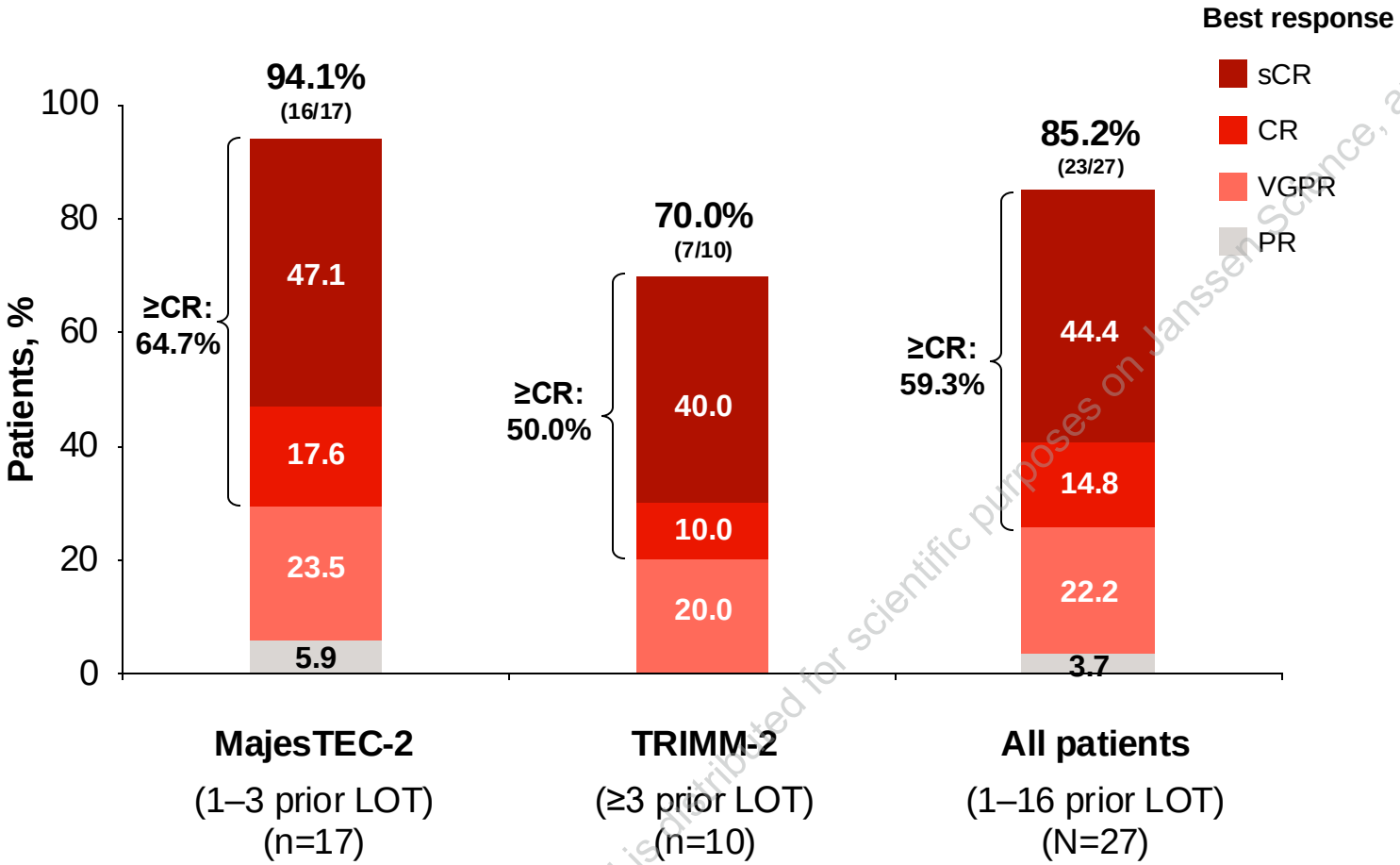
	MajesTEC-2 (1–3 prior LOT); n=17		TRIMM-2 (≥3 prior LOT); n=10		All patients; N=27	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Any infection	16 (94.1)	11 (64.7)	9 (90.0)	6 (60.0)	25 (92.6)	17 (63.0)
Infections[a]						
Upper respiratory tract infection	8 (47.1)	0	4 (40.0)	0	12 (44.4)	0
Pneumonia	4 (23.5)	1 (5.9)	4 (40.0)	4 (40.0)	8 (29.6)	5 (18.5)
Sinusitis	4 (23.5)	0	4 (40.0)	1 (10.0)	8 (29.6)	1 (3.7)
COVID-19	3 (17.6)	1 (5.9)	4 (40.0)	1 (10.0)	7 (25.9)	2 (7.4)
COVID-19 pneumonia	4 (23.5)	4 (23.5)	1 (10.0)	1 (10.0)	5 (18.5)	5 (18.5)
Hypogammaglobulinemia						
Hypogammaglobulinemia[b]	16 (94.1)		10 (100)		26 (96.3)	
Received IVIG[c]	12 (70.6)		8 (80.0)		20 (74.1)	

- 6 patients died due to infections
  - 4 due to COVID-19 pneumonia[d]
  - 1 due to pneumonia[e]
  - 1 due to pseudomonal bacteremia[f]
- 4 of these 6 patients had hypogammaglobulinemia at time of death and were not receiving Ig replacement before onset of the infection
- 1 additional patient died due to PD

No fatal infections occurred following implementation of intensified infection prophylaxis, including Ig replacement

[a]Infections in ≥15% of patients. [b]Hypogammaglobulinemia reported as an AE or postbaseline IgG <400 mg/dL. [c]Study enrollment began before IVIG was routinely recommended for patients treated with bispecific antibodies (MajesTEC-2, Mar 2021 to Aug 2021; TRIMM-2, Nov 2020 to Mar 2021). [d]MajesTEC-2, n=3; TRIMM-2, n=1. 1 case of COVID-19 death was reported as lung infection with COVID-19 as the causative pathogen; 2 of these 4 fatal COVID-19 pneumonia events qualified as TEAEs leading to treatment discontinuation. [e]TRIMM-2. [f]MajesTEC-2. AE, adverse event; Dara, daratumumab; Ig, immunoglobulin; IgG, immunoglobulin G; IVIG, intravenous immunoglobulin; LOT, line of therapy; PD, progressive disease; Pom, pomalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab.

Tec-Dara-Pom in MajesTEC-2 and TRIMM-2: Response Rates



- Tec-Dara-Pom demonstrated rapid and deep responses across both cohorts
  - ORR: 85.2%
  - ORR: 72.7% in Dara-exposed patients[a]
- Deeper responses in 1–3 vs ≥3 prior LOT
  - ≥CR: 64.7% vs 50.0%
  - ≥VGPR: 88.2% vs 70.0%
- Median times to first and best response in all patients were 1.0 month and 3.2 months, respectively[b]

Response was assessed by investigators, based on International Myeloma Working Group criteria. Percentages were calculated with the number of patients in each group as the denominator. [a]n=8/11. [b]n=23.
CR, complete response; Dara, daratumumab; LOT, line of therapy; ORR, overall response rate; Pom, pomalidomide; PR, partial response; sCR, stringent complete response; Tec, teclistamab; VGPR, very good partial response.

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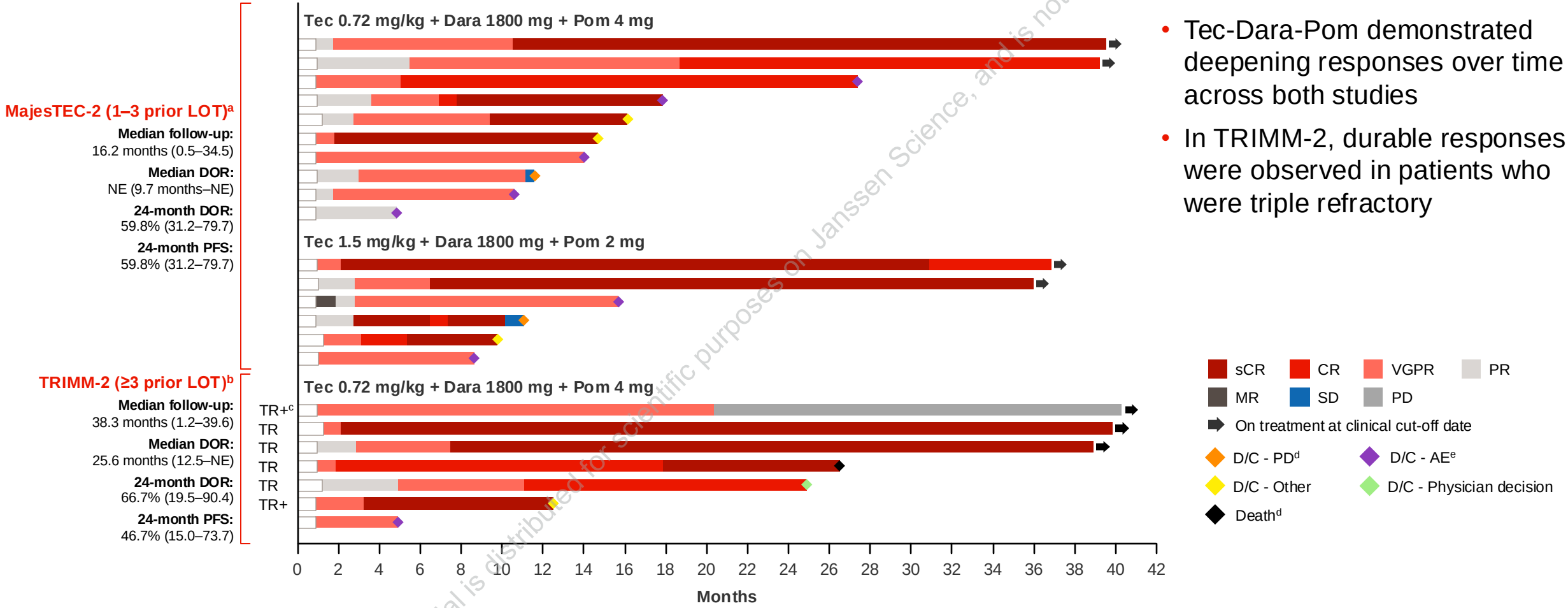
Tec-Dara-Pom in MajesTEC-2 and TRIMM-2: Treatment Duration in Responders



- Tec-Dara-Pom demonstrated deepening responses over time across both studies
- In TRIMM-2, durable responses were observed in patients who were triple refractory

Follow-up assessments will be conducted for up to 16 weeks after the last dose of study treatment. [a]n=16; clinical cut-off date Aug 22, 2024. [b]n=7; clinical cut-off date Apr 10, 2024. [c]Patient had PD per International Myeloma Working Group criteria (bone lesions) and remained on study treatment based on investigator decision following local radiation. [d]PD and deaths occurring beyond end of treatment are not represented in the figure. [e]Discontinuation due to AEs includes non–treatment-emergent events. +, penta-refractory; AE, adverse event; CR, complete response; D/C, discontinued (patients considered as discontinuing treatmentwhen all study drugs have been discontinued); Dara, daratumumab; DOR, duration of response; LOT, line of therapy; MR, minimal response; NE, not estimable; PD, progressive disease; PFS, progression-free survival; Pom, pomalidomide; PR, partial response; sCR, stringent complete response; SD, stable disease; Tec, teclistamab; TR, triple refractory (≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 monoclonal antibody); VGPR, very good partial response.

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Tec-Dara-Pom in MajesTEC-2 and TRIMM-2: Conclusions

- Tec-Dara-Pom is feasible with promising efficacy at >2 years' follow-up in patients with RRMM, including in Dara-exposed patients
- Intensified recommendations for Ig replacement and infection prophylaxis may have improved the infection profile of Tec-Dara-Pom, with no additional fatal infections reported after implementation
- High rate of deep responses, which improved in earlier LOT
  - Overall: ORR 85.2%, ≥CR 59.3%
  - 1–3 prior LOT: ORR 94.1%, ≥CR 64.7%
  - ≥3 prior LOT: ORR 70.0%, ≥CR 50.0%
- Longer DOR and PFS in less heavily pretreated patients
  - 1–3 prior LOT: median DOR NE; 24-month PFS 59.8%
  - ≥3 prior LOT: median DOR 25.6 months; 24-month PFS 46.7%

CR, complete response; Dara, daratumumab; DOR, duration of response; Ig, immunoglobulin; LOT, line of therapy; NE, not estimable; ORR, overall response rate; PFS, progression-free survival; Pom, pomalidomide; RRMM, relapsed/refractory multiple myeloma; Tec, teclistamab.

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Tec + Dara + IMiDs: Additional Data at ASH 2024 Supporting Further Evaluation in Earlier Treatment Lines

Presented

Tec-DRd or Tec-DVRd

Phase 2 MajesTEC-5 study (GMMG-HD10/DSMM-XX)

NCT05695508

Raab MS, et al

Presented December 8, 2024 (Oral Presentation #493)

To be presented

Tec-Dara-Pom

Phase 1b MajesTEC-2 study
NCT04722146

Vishwamitra D, et al

Oral presentation #594, December 8, 2024
1:15–1:30 PM

Marriott Marquis San Diego Marina
San Diego Ballroom AB

Tec-Dara-Len

Phase 1b MajesTEC-2 study
NCT04722146

Cortes-Selva D, et al

Poster presentation #4653, December 9, 2024
6:00–8:00 PM

San Diego Convention Center
Halls G-H

Dara, daratumumab; DRd, daratumumab, lenalidomide, and dexamethasone; DVRd, daratumumab, bortezomib, lenalidomide, and dexamethasone; IMiD, immunomodulatory drug; Len, lenalidomide; Pom, pomalidomide; Tec, teclistamab.

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https://www.congresshub.com/ASH2024/Oncology/Teclistamab/DSouza

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